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EVALUATION OF NOOTROPIC ACTIVITY OF *SEMECARPUS ANACARDIUM* LEAVES IN RODENTS

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Keywords:

Nootropic, Shuttle box, Elevated plus-maze, Alzheimer, Piracetam

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ABSTRACT: Evaluation of nootropic activity of *Semecarpus anacardium* leaves ethyl alcohol extract on exteroceptive behavior and interoceptive behavior was investigated by use of Shuttle box, Continuous Avoidance Response Apparatus and Elevated plus-maze test, Scopolamine-induced amnesia, Diazepam-induced amnesia, and Sodium nitrite-induced amnesia. The beha-vioral study was done using Lithium- induced head twitches (5-HT mediated behavior) test. The ethyl alcohol leaves extract was administered orally in two different dosages to male albino rats (100 and 200 mg/kg daily, p.o. & isolated flavonoid 40 mg/kg daily p.o) and Swiss albino mice (100 and 200 mg/kg Daily p.o. & isolated flavonoid 40mg/kg daily p.o). The result was compared to piracetam (100 mg/kg, p.o) used as a standard drug. The buzzer (conditioned stimulus) and an electric shock (unconditioned stimulus, 30 v and 0.5 sec) were used in the Shuttle box. The ethyl alcohol extract of *Semecarpus anacardium* leaves showed statically significant improvement in memory retention and learning when compared to control. The study shows that the ethyl alcohol extract of *Semecarpus anacardium* leaves has the dose-dependent cholinergic activity to improve memory. In light of the above, it may be worthwhile to explore the potential of *Semecarpus anacardium* in the management of Dementia patients.

INTRODUCTION: In 1972 Corneliu Giurgea coined the term nootropic to describe a new class of molecules that selectively acted towards the higher-level integrative activity of the brain [1-3]. Nootropics are cognitive enhancer drugs or supplements that improve the mental action or process of acquiring knowledge, memory, executive function, judgment, reasoning, problem-solving and decision making. Nootropics can be divided into three categories: Synthetic compounds, dietary supplements and prescription drugs.

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Prescription drugs like stimulants are suggested for attention deficit hyperactivity disorder (ADHD) or donepezil for Alzheimer's. Problems with memory, thinking and behavior are caused by Alzheimer's disease. Nootropics act probably by altering the neurotransmitter, hormone and enzyme levels that are present in the brain by increasing the oxygen supply or nerve growth stimulation of brains. Herbs may increase the level of acetylcholine and also increase blood flow towards the brain. The class of drugs that's share pyrrolidone nucleus such as piracetam is a class of Racetams which is considered as nootropics [4-5].

There is a lot of research that has been done for the treatment of Alzheimer's disease and the other brain-related disease after doing the literature survey of different herbal drugs leaves of *Semacarpus anacardium* was selected for study [6].

Semacarpus anacardium contains a variety of phytoconstituents as phenolic compounds, vitamins, bioflavonoids, bhilawanols. The extract of fruit and nut shows antioxidant, CNS stimulant, hypoglycemic, anticarcinogenic activity [7].

MATERIALS AND METHODS:

Drugs and Chemicals: Piracetam ('Neurocetam syrup" Brown and Burk, India), Scopolamine ('Hyoscine' German Remedies, India), Diazepam ('Calmpose' Ranbaxy, India), Lithium carbonate ('Licab' Torrent, Solan, India.), Phenytoin (Sigma, USA), Sodium Nitrite (Sd fine-chemicals, Mumbai) and *Semecarpus anacardium* were used for the present study.

Preparation of Plant Extract: Leaves of *S. anacardium* were collected from forest of Betul MP and were authenticated by Dr. A. K Pathak Professor (Head) & new voucher Specimen Bot H-02/53/118 was deposited at the herbarium of Department of Pharmacy, Barkatullah University, and Bhopal. The leaves powder of *Semecarpus anacardium* (500 gm) were defatted with petroleum ether, then extracted with 1000 ml ethyl alcohol (40-45 °C) by Soxhlet extraction for 8 h. The extracts obtained were later kept for evaporation to remove the excessive solvents. Further it is isolated f**o**r its lead bioactive compound by column chromatography. The dried extract & isolated flavonoid (DKT-SA) were taken and daily prepared freshly for feeding animals by mixing the extract with 2% gum acacia and 100 ml water and triturated.

Experimental Animals: Albino rats (Wistar strain) of both sex (weighing 150-200 g) and Albino mice of either sex (weighting 20-30 g) were procured from the Central Animal House of Pinnacle Biomedical Research Institute Bhopal (MP). The animals were acclimatized for seven days under laboratory conditions [8, 9]. The animals were fed with a commercially available rat pellet diet. Water was allowed *ad libitum* under strict hygienic conditions.

The study protocols were duly approved by the Institutional Animal Ethics Committee (IAEC) of Pinnacle Biomedical Research Institute Bhopal (MP). Studies were performed in accordance with the CPCSEA guidelines (Proposal No -4127).

Determination of Acute Toxicity (LD_{50}): The acute toxicity of *Semecarpus anacardium* was determined by using female albino mice (20-30 g). The animals were fasted for 4 h prior to the experiment and up and down procedure (OECD guideline no. 425) method of CPCSEA was adopted for acute toxicity studies [10].

Animals were administered with daily 0.1 ml of *Semecarpus anacardium* leaves extract and observed for its mortality during 48 h study period (short term) toxicity. Based on the short-term profile of drug, the dose for the next animals was determined as per as OECD guideline 425. All the animals were observed for long term toxicity (0.1 ml, daily for 25 days). *Semecarpus anacardium* did not produce any obvious toxicity or mortality when subjected to chronic toxicity studies for 25 days in mice according to OECD guidelines. Hence, the formulation was ensured to be devoid of any potential toxicity and obvious mortality. Further, the different doses of *Semecarpus anacardium* used in the study for evaluation of its nootropic activity were decided based on laboratory experience. Thus the doses 100 mg/kg, 200 mg/kg & isolated flavonoid (DKT-SA) 40 mg/kg p.o. were used as low and high doses, respectively [11].

Exteroceptive Behavior Models:

Active Avoidance Paradigm (Shuttle Box): [12-16]

Group I was maintained as normal control, which was given with distilled water only daily once for 14 days. Group II with piracetam (200 mg/kg, p.o.), which served as standard. Groups III, IV, V, were treated with different doses of *Semecarpus anacardium* (100 and 200 mg/kg p.o.) and isolated flavonoids DKT-SA (40mg p.o.) respectively for 14 days. All groups of rats were trained upto 100% learning criterion of active avoidance response. During the training period, each rat was placed in one of the two chambers of the Sidman box, and after 5 sec the buzzer (conditioned stimulus, CS) was sounded for 2 sec, followed by an electric shock (unconditioned stimulus, UCS; 30v, 0.5 sec) through the grid floor. Thereafter, a rest-pause of 180 sec was allowed. If the rat jumped within the CS duration to the unelectrified safe box, so as to avoid the UCS, it was allowed to rest there for next 30 sec. However, if the rat did not show, the avoidance response was removed from the shock chamber after 180 sec and was initiated for the next

trial. The rat was given 10 trials daily until they reached the 100% criterion of active avoidance response. After an interval of 15 days, the rats were subjected to a repeat test with the treatment of different doses of the *Semecarpus anacardium* in order to assess the retention of the previously learned active avoidance response. Similarly, Nootropic activity of the standard drug was evaluated.

Passive Avoidance Paradigm: [17-25] The memory-impairing dose of phenytoin 25mg/kg daily for 14 days and the selected dose of *Semecarpus anacardium* for 07 days, *i.e.,* on 8th to 14th day, and the parameters mentioned above were noted. Group I was maintained as normal control, which was given with distilled water, Group II with Phenytoin alone (25 mg/kg, p.o.) daily once for 14 days. Group III with piracetam (200 mg/kg, p.o.), which served as standard, Groups IV, V, and VI, were treated with different doses of *Semecarpus anacardium* (100 and 200 mg/kg, p.o.) and isolated flavonoids DKT-SA (40mg p.o.) respectively for 7 days as mentioned above. Passive-avoidance task is a method widely used for screening drugs affecting learning and memory.

The method described by Papazova *et al.,* (1994) was modified as follows. An inverted petridish placed in the center of the grid floor of a continuous avoidance apparatus was used. The petridish served as the shock-free zone (SFZ). Mice were placed in the SFZ and upon stepping down from the SFZ were given an electric shock (20 V) through the grid floor. Animals were trained to remain on the SFZ for at least 60 sec and mice which did not meet these criteria in five trials were rejected. Observations were made for acquisition *i.e.,* the number of trials required to reach the learning criteria and for retention of learning for 10 min at 2 h and 24 h post-training. The following retention parameters like step-down latency (SDL) in seconds, step-down error (SDE) as the number of times the animal stepped down from the SFZ, and the time spent in the shock zone (TSZ) in seconds are noted.

FIG. 1: ACTIVE AVOIDANCE PARADIGMS (SHUTTLE BOX)

FIG. 2: PASSIVE AVOIDANCE PARADIGM (CONTINUOUS AVOIDANCE RESPONSE APPARATUS)

Elevated Plus-maze Model: The Elevated plus-maze apparatus used in this model consisting of two open arms (16 cm × 5 cm) and two closed arms (16 cm × 5 cm × 12 cm).

The arms extended from a central platform (5 cm × 5 cm), and the maze is elevated to a height of 25 cm from the floor. Group I was maintained as normal control, which was given with distilled water for 7 days. Group II with piracetam (200 mg/kg, p.o.), which served as standard, Groups III, IV, V was treated with different doses of *Semecarpus anacardium* (100 and 200 mg/kg p.o.) and isolated flavonoids DKT-SA (40 mg p.o.) respectively for 7 days [17, 18, 20, 26, 27-30]. On the 7th day, 90 min after the above treatment, each mouse was placed at the end of an open arm of EPM facing away from the central platform.

TL (Transfer latency) was recorded *i.e.*, the time taken by the mouse to move into one of the enclosed arms with all its four legs. If the animal did not enter into one of the enclosed arms within 90 s, it was gently pushed into one of the two enclosed arms, and the TL was assigned as 90 s. The mouse was allowed to explore the maze for the next 10 s and then returned to its home cage. Retention of this learned-task was examined 24 h after the 7th-day trial. The inflexion ratio was calculated by the formula as follows[16]. Inflexion ratio (IR) = $(L_0 - L_1)/ L_0$, where L_0 is the initial TL (s) on first day and L_1 is the TL (s) on the 2nd day.

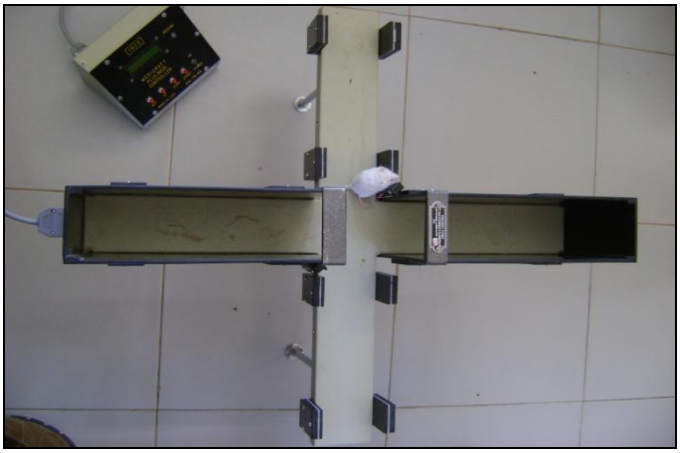

FIG. 3: ELEVATED PLUS MAZE

Interceptive Behavior Models:

Scopolamine-induced Amnesia: [17, 18] Group I was maintained as normal control, which was given with, distilled water, Group II with Scopolamine (1.0 mg/kg, i.p.) alone. Group III with piracetam (200 mg/kg, p.o.), which served as standard, Groups IV, V, VI, were treated with different doses of *Semecarpus anacardium* (100 and 200 mg/kg, p.o.) and isolated flavonoids DKT-SA (40 mg p.o.) respectively for 14 days as mentioned above.

All groups were treated accordingly as mentioned above for a period of 14 days, and Scopolamine was given (1 mg/kg, i.p.) 90 minutes after the last dose of standard and *Semecarpus anacardium* to induce impairment of memory through muscuranic system. Transfer latency (TL) was recorded 45 min and 24 hrs after injection of scopolamine using Elevated Plus maze (EPM). The inflexion ratio was calculated as described earlier **Fig. 3.**

Diazepam-induced Amnesia: [17, 20] Group I was maintained as normal control, which was given with, distilled water, Group II with Diazepam alone (1 mg/kg, i.p.) alone. Group III with piracetam (200 mg/kg, p.o.) which served as standard, Groups IV, V, VI was treated with different doses of *Semecarpus anacardium* (100 and 200 mg/kg p.o.) and isolated flavonoids DKT-SA (40 mg p.o.) respectively for 14 days as mentioned above.

All groups were treated respectively as mentioned above for a period of 14 days, and Diazepam 1 mg/kg was given i.p. 90 minutes after last dose of standard/*Semecarpus anacardium* to induce impairment of memory that act through GAB Aergic system. Transfer latency (TL) was recorded with Elevated Plus maze (EPM) at 45 min and 24 h after injection of Diazepam. The inflexion ratio was calculated as described earlier **Fig. 3.**

Sodium Nitrite-induced Amnesia: [18] Group I was maintained as normal control, which was given with, distilled water, Group II with Sodium nitrite alone (25 mg/ kg, s.c) alone. Group III with piracetam (200 mg/kg, p.o.), which served as standard, Groups IV, V, VI was treated with different doses of *Semecarpus anacardium* (100 and 200 mg/kg, p.o.) and isolated flavonoids DKT-SA (40mg p.o.) Respectively for 14 days as mentioned above. All groups were treated according to protocol for a period of 7 days and sodium nitrite 25 mg/ kg was given s.c. route 90 minutes after the last dose. Thereafter using Elevated Plus maze (EPM), Transfer latency (TL) will be recorded at 45 min and 24 h after administration of Sodium nitrite. The inflexion ratio was calculated as described earlier **Fig. 3.**

Behavioral Study:

Lithium-induced Head Twitches (5-HT Mediated Behavior): [19, 31] Group I was maintained as normal control, which was given with distilled water (10ml/kg, p.o.), Group II with Lithium alone (190mg/kg i.p.), daily once for 7 days, Group III with Piracetam (200 mg/kg, p.o.) which served as standard, Group IV with Amitriptyline (20mg/kg, p.o.) which served as standard, Groups V, VI and VII were treated with different doses of *Semecarpus anacardium* (100 and 200 mg/kg p.o.) and isolated flavonoids DKT-SA (40mg p.o.) respectively for 7 days as mentioned above. Lithium induced head twitching is used to assess the effect of drugs influencing second messenger system like Phosphatidylinositol (PI) pathway (5-HT receptor). Rats were treated with vehicle / formulation *Semecarpus anacardium* / Piracetam 30 min before i.p. administration of 190mg/kg of lithium carbonate and the number of head twitches was counted up to 60 min after lithium treatment and prevention of head twitches due to standard drug and *Semecarpus anacardium* was recorded.

Metabolic Influence:

Sodium Nitrite Intoxication: [24] Group I was maintained as normal control, which was given with distilled water (10 ml/kg, p.o.), Group II with Sodium nitrite alone (250 mg/ kg s.c.) daily once

for 7 days Group III with piracetam (200 mg/kg, p.o.) which served as standard, Groups IV, V, VI was treated with different doses of *Semecarpus anacardium* (100 and 200) mg/kg p.o.) And isolated flavonoids DKT-SA (40 mg p.o.) respectively for 7 days as mentioned above. All the groups were treated according to the protocol for a period of 7 days, and sodium nitrite 250 mg/kg was given s.c. 60 min after the last dose of standard/ polyherbal formulation to induce chemical hypoxia. Sodium nitrite reduces the oxygen-carrying capacity of the blood by converting hemoglobin to methaemoglobin, and cessation of respiration time in each group was recorded.

Statistical Analysis: The results are expressed as the mean ± SEM. The results obtained from the present study were analyzed using one-way ANOVA followed by Dunnett's multiple comparison tests. Data was computed for statistical analysis by using Graph Pad PRISM Software.

RESULTS AND DISCUSSION:

Determination of Acute Toxicity (LD_{50}): *Semecarpus anacardium* was subjected to toxicity studies according to OECD guidelines. The formulation did not produce any toxicity even at the highest dose selected (0.1ml, daily for 25 days). Hence, the formulation is free from any obvious toxicity when used multiple folds of its recommended dose for humans.

Determination of Nootropic Activity:

Exteroceptive Behavior Models:

Active Avoidance Learning and Retention in Rats: Effect of *Semecarpus anacardium* on learning and retention was studied using Active avoidance paradigm (Shuttle box) apparatus. Piracetam (200 mg/kg) and different doses of *Semecarpus anacardium* (100 and 200 mg/kg) and isolated flavonoids DKT-SA (40 mg p.o.) treated groups had shown a decrease in time spent in shock zone and number of shocks. Statistically significant reduction in trials and shocked trials for relearning were observed with piracetam and *Semecarpus anacardium* **Table 1.**

Passive Avoidance Learning and Retention in Mice: Effect of *Semecarpus anacardium* on learning and retention was tested using continuous avoidance response apparatus. Piracetam (200 mg/kg) and different dose levels of *Semecarpus anacardium* (100 and 200 mg/kg) and isolated flavonoids DKT-SA (40mg p.o.) treated groups had shown increased Step-down latency and decreased time spent in shock zone and number of errors. Statistically significant increase in SDL and reduction in TSZ and no. of errors were observed with piracetam and *Semecarpus anacardium* **Table 2.**

Inflexion Ratio in Mice (EPM Model): Effect of *Semecarpus anacardium* on inflexion ratio was recorded with Elevated plus-maze apparatus. In mice, Piracetam (200 mg/kg) and different dose levels of *Semecarpus anacardium* (100 and 200 mg/kg) and isolated flavonoids DKT-SA (40 mg p.o.) treated groups had shown an increase in IR. Statistically significant reduction in TL was observed with piracetam and *Semecarpus anacardium* **Table 3**.

Interoceptive Behavior Models:

Inflexion Ratio in Mice (Scopolamine-induced Amnesic Model): Scopolamine treated group of mice exhibits impairment of memory and decrease in IR as compared to the normal control group, which indicates the induction of amnesia. Piracetam and all the doses of *Semecarpus anacardium* treated groups had shown increased IR, significant reduction in TL, and reversed the scopolamine- induced amnesia **Table 4.**

Inflexion Ratio in Mice (Diazepam-induced Amnesic Model): Diazepam has induced dose-dependent amnesia, and in this amnesic model, a decrease in IR was observed when compared to the normal control group. Piracetam and all doses of *Semecarpus anacardium* treated groups had exhibited a highly significant nootropic activity with an increased IR & reduction in TL observed with EPM and reversed the diazepam-induced amnesia. Statistically significant reduction in TL was observed in piracetam, and *Semecarpus anacardium* treated groups **Table 5.**

Inflexion Ratio in Mice (Sodium Nitrite-induced Amnesic Model): Sodium nitrite induces impairment of memory; and in this model sodium nitrite treated group has shown a decrease in IR as compared to the normal control group, which indicates the induction of amnesia.

Piracetam and all the doses of *Semecarpus anacardium* treated groups had shown increased IR and a significant reduction in TL and reversed the sodium nitrite-induced amnesia. Statistically significant reduction in TL was observed with piracetam and *Semecarpus anacardium* **Table 6**.

Behavioral Study:

Lithium-induced Head Twitches in Rats: Lithium treated group had shown 20.333 ± 1.308 head twitches. Prior treatment with piracetam decreased the number of head twitches to 3.167 ± 0.4014, and all doses of *Semecarpus anacardium* 100 and 200 mg/kg and isolated flavonoids DKT-SA (40mg p.o.) had shown a significant reduction in head twitches *i.e.,* 11.167 ± 0.4014, 7.830 ± 0.4014 and 4.167 ± 0.4014 respectively. A significant nootropic effect was observed with piracetam, and different doses of *Semecarpus anacardium* treated groups. Amitriptyline had reduced the head twitches to 1.833 ± 0.4014 **Table 7**.

Metabolic Influence:

Sodium Nitrite in Toxication Model in Mice: The sodium nitrite treated group had shown 13.66 ± 0.350 min for a cessation of respiration. Prior treatment with piracetam and different doses of *Semecarpus anacardium* (100 and 200 mg/kg) and isolated flavonoids DKT-SA (40 mg p.o.) had shown increased time for cessation of respiration to 32.5 ± 0.50, 21.25 ± 0.220, 23.76 ± 0.14 and 27.91 ± 0.200 min respectively. However, a significant effect was observed with piracetam, and different doses of *Semecarpus anacardium* as compared with sodium nitrite alone treated group **Table 8**.

CONCLUSION: In the present study, we have focused upon exploring the potential of *Semecarpus anacardium* in reversing the memory deficits and improving acquisition and memory retention in experimental animals. Three exteroceptive models were used for evaluation of nootropic activity with *Semecarpus anacardium*, and it has shown a significant effect on learning and memory processes, which were indicated by decreased time spent in shock zone and number of errors in the active avoidance model, increased Step-down latency (SDL), decreased time spent in shock zone & number of errors in passive avoidance paradigm and increased inflexion ratio in EPM. In the interoceptive model, it has reversed the amnesia induced by scopolamine, diazepam and sodium nitrite. In the lithium-induced head twitches model, all the doses of *Semecarpus anacardium* (100 and 200 mg/kg) & isolated flavonoids DKT-SA 40 mg/kg have shown a significant reduction in head twitches, which indicates that *Semecarpus anacardium* might be interfering with a 5-HT transmission[13] and antagonizing the effect of lithium. In the sodium nitrite intoxication model, all the doses of *Semecarpus anacardium* (100 and 200 mg/kg) isolated flavonoids DKT-SA 40 mg/kg has shown a significant increase in the cessation of respiration time. In the light of the above, it may be worthwhile to explore the potential of *Semecarpus anacardium* in the management of Dementia patients.

TABLE 1: EFFECT OF S. ANACARDIUM ON ACTIVE AVOIDANCE LEARNING AND RETENTION IN RATS (MEAN ± SEM)

Group no.	Treatment	Dose (per kg)	Number of Shocks			Time Spent in Shock Zone (in sec)		
			Learning Acquisition	Relearning	Retaining	Learning Acquisition	Relearning	Retaining
			1st day	15th day	16th day	1st day	15th day	16th day
I	Control(vehicle)	10 ml/kg p.o.	7.50±1.049	5.83±0.753	5.33±0.516	15.50±1.033	13.67±1.033	10.50±0.47
II	Piracetam	200 mg/kg p.o.	7.33±1.366	2.67±0.816	0.50±0.548	15.17±1.472	5.17±0.983	2.00±0.632
III	*Semecarpus anacardium*	100mg/kg p.o.	6.83±1.169	2.83±0.753	2.00±0.632	15.50±1.378	12.17±1.169	8.67±1.033
IV	*Semecarpus anacardium*	200 mg/kg p.o	7.00±0.894	2.50±0.548	1.67±0.516	15.83±0.753	6.17±0.753	3.63±0.516
V	*DKT-SA*	40 mg/kg p.o	6.40 ±1.517	1.83±0.753	0.83±0.753	15.50 ±1.643	5.50±0.548	2.33±0.516
	F		0.75±29	27.215±29	61.671±29	0.194±29	115.488±29	205.471±29
One-way ANOVA		D_f						

n=6 in each group. Data are expressed as mean ±SEM. Statistical analysis by one-way ANOVA followed by Dunnett's't' test Significance at P<0.05* and NS-not significant vs. control group

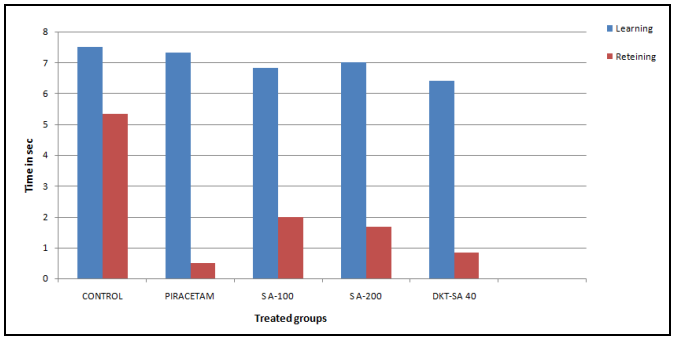

FIG. 4: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. A.* ON NO. OF SHOCK IN MICE (PASSIVE AVOIDANCE PARADIGM)

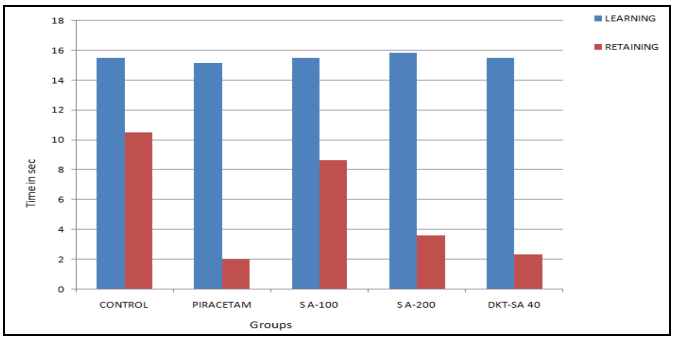

FIG. 5: HISTOGRAM SHOWING THE EFFECT OF S. A. ON TSZ (ACTIVE AVOIDANCE) IN RATS

TABLE 2: EFFECT OF *S. ANACARDIUM* ON PASSIVE AVOIDANCE LEARNING AND RETENTION IN MICE (MEAN ± SEM)

Group no.	Treatment	Dose (per Kg)	No. of trials for acquisition	Step-Down Latency (SDL)		Time Spent In Shock Zone (TSZ)		Step-Down Error (SDE)	
				Learning	Retention	Learning	Retention	Learning	Retention
I	Control	10 ml p.o.	2.83	14.83±0.753	87.17±1.329	47.67±0.816	17.00±0.894	6.17±0.753	3..17±0.408
II	Phenytion	25 mg p.o.	3.50	13.67±1.033^{NS}	85.50±1.378	47.00±0.632	16.83±1.169	6.00±0.894	3.67±0.516
III	Piracetam	200 mg p.o	3.83	92..83±0.983*	281.33±3.830*	16.83±1.169	3.83±0..753	2.33±0.516	1.17±1.169
IV	*Semecarpus anacardium*	100 mg/kg p.o.	2.83	49.50±1.378*	204.83±3.817*	28.00±1.673	6.67±1.211	3.50±0.548	0.83±0.753
V	*Semecarpus anacardium*	200 mg/kg p.o.	3.17	73.50±1.57*	276.50±6.058*	17.17±1.169	6.50±1.049	2.33±1.03*	1.67±0.576
VI	DKT-SA	40 mg / kg p.o.	3.50	86.00±0.66*	282.83±5.672*	12.50±0.837	5.17±0.983	2.67±0.816	1.17±0.753
F One-way ANOVA d_f				5919.8705	3193.1915	1213.4885	204.20935	31.75335	15.42835

n=6 in each group. Data are expressed as mean ± SD. Statistical analysis by one-way ANOVA followed by Dunnett's't' test Significance at P<0.05* and NS-not significant *vs.* control group.

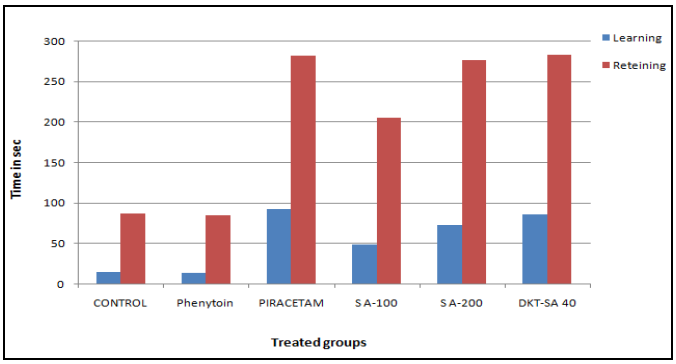

FIG. 6: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. A.* ON SDL IN MICE (PASSIVE AVOIDANCE)

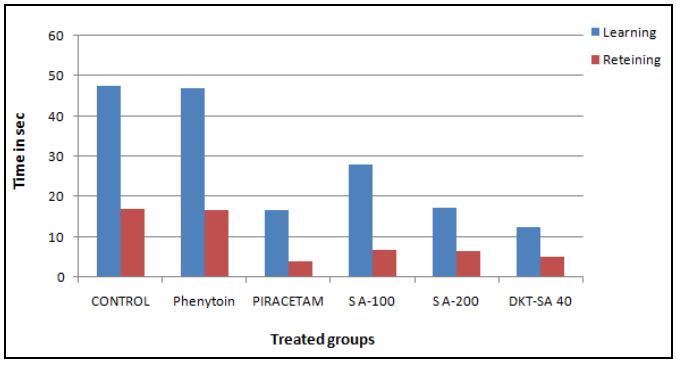

FIG. 7: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. A.* ON TSZ IN MICE (PASSIVE AVOIDANCE PARADIGM

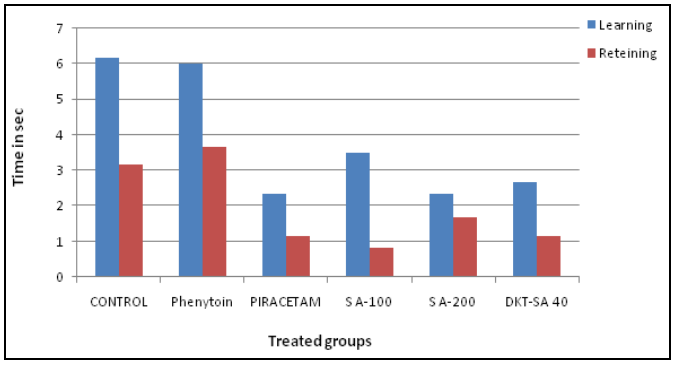

FIG. 8: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. A.* ON SDE IN MICE (PASSIVE AVOIDANCE PARADIGM)

TABLE 3: EFFECT OF *S. ANACARDIUM* ON INFLEXION RATIO IN MICE (EPM MODEL)

Group no.	Treatment	Dose (Per kg)	Inflexion Ratio (Mean ± Sem)
I	Control(vehicle)	10 ml p.o.	0.2987± 0.011
II	Piracetam	200 mg p.o.	0.7016**±0.007
III	*S. anacardium*	100 mg p.o.	0.4407**±0.0156
IV	*S. anacardium*	200mg p.o.	0.6026**±0.00902
V	*DKT-SA*	40mg p.o.	0.6934**±0.0299
	F One-way ANOVA Df		107.82 29

n=6 in each group. Data is expressed as mean ±SEM. Statistical analysis by one-way ANOVA followed by Dunnett's't' test. Significance at P<0.05*, P <0.01** and ns-not significant *vs.* control group.

TABLE 4: EFFECT OF *S. ANACARDIUM* ON INFLEXION RATIO IN MICE (SCOPOLAMINE-INDUCED AMNESIC MODEL)

Group no.	Treatment	Dose (Per kg)	Inflexion Ratio(Mean ± Sem)
I	Normal control (vehicle)	10 ml p.o.	0.2681^{ns} ± 0.02676
II	Scopolamine control	1.0 mg i.p.	0.1623 ± 0.04422
III	Piracetam	200 mg p.o.	0.6570** ± 0.008616
IV	*S. anacardium*	100 mg p.o.	0.3843** ± 0.03990
V	*S. anacardium*	200 mg p.o.	0.6355** ± 0.04614
VI	*DKT-SA*	40 mg p.o.	0.6314** ± 0.03261
	F One-way ANOVA d_f		36.66835

n=6 in each group. Data is expressed as mean ±SEM. Statistical analysis by one-way ANOVA followed by Dunnett's't' test. Significance at P<0.05*, P <0.01** and ns-not significant *vs.* control group.

TABLE 5: EFFECT OF *S. ANACARDIUM* ON INFLEXION RATIO IN MICE (DIAZEPAM-INDUCED AMNESIC MODEL)

Group no.	Treatment	Dose(Per ng)	Inflexion Ratio (Mean ± Sem)
I	Normal control (vehicle)	10 ml p.o.	0.3464^{ns} ± 0.05074
II	Diazepam alone	1.0 mg i.p.	0.2821 ± 0.04446
III	Piracetam	200 mg p.o.	0.6594**± 0.02429
IV	*S. Anacardium*	100 mg p.o.	0.4218* ± 0.02115
V	*S. Anacardium*	200 mg p.o.	0.5113** ± 0.02583
VI	*DKT-SA*	40 mg p.o.	0.6395** ± 0.02084
	F One-way ANOVA d_f		21.33635

n=6 in each group. Data is expressed as mean ±SEM. Statistical analysis by one-way ANOVA followed by Dunnett's't' test. Significance at P<0.05*, P <0.01** and ns-not significant *vs.* control group.

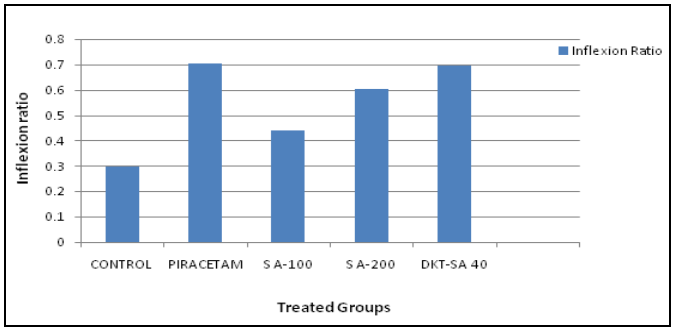

FIG. 9: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. ANACARDIUM* ON INFLEXION RATIO IN MICE (EPM MODEL)

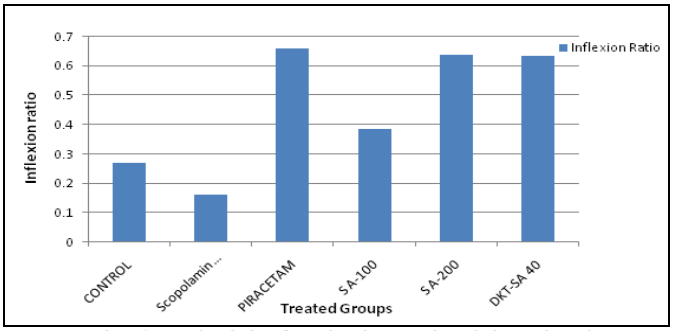

FIG. 10: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. ANACARDIUM* ON SCOPOLAMINE INDUCED AMNESIA IN MICE (EPM MODEL)

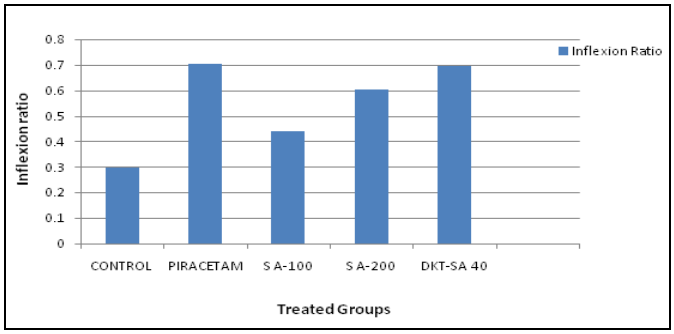

FIG. 11: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. ANACARDIUM* ON DIAZEPAM- INDUCED AMNESIA IN MICE (EPM MODEL)

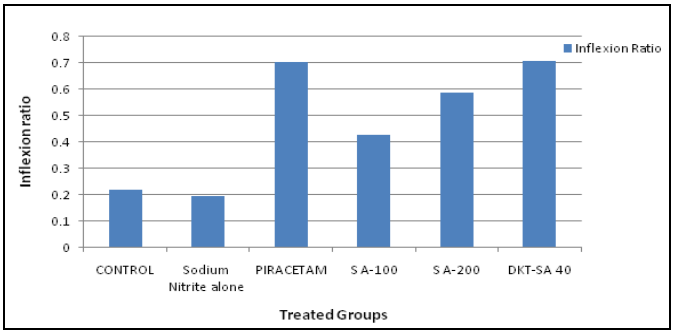

FIG. 12: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. ANACARDIUM* ON SODIUM NITRITE- INDUCED AMNESIA IN MICE (EPM

TABLE 6: EFFECT OF *S. ANACARDIUM* ON INFLEXION RATIO IN MICE (SODIUM NITRITE-INDUCED AMNESIC MODEL)

Group no.	Treatment	Dose (Per kg)	Inflexion Ratio (Mean ± Sem)
I	Normal control (vehicle)	10 ml p.o.	0.2211^{ns}±0.093
II	Sodium nitrite alone	1.0 mg i.p.	0.1943±0.025
III	Piracetam	200 mg p.o.	0.7043**±0.043
IV	*S. anacardium*	100 mg p.o.	0.4278*±0.080
V	*S. anacardium*	200 mg p.o.	0.5889**±0.049
VI	*DKT-SA*	40 mg p.o.	0.7075**±0.016
	F One-way ANOVA d_f		15.69435

n=6 in each group. Data is expressed as mean ±SEM. Statistical analysis by one-way ANOVA followed by Dunnett's't' test. Significance at P<0.05*, P <0.01** and ns-not significant *vs* control group.

TABLE 7: EFFECT OF *S. ANACARDIUM* ON LITHIUM-INDUCE HEAD TWITCHES IN RATS

Group no.	Treatment	Dose (Per kg)	No. of Head Twitches for 60 min Session (Mean ± Sem)
I	Normal control (vehicle)	10 ml p.o.	-
II	Lithium control	190 mg i.p.	16.333±0.7149
III	Piracetam	200 mg p.o.	3.167**± 0.4014
IV	Amitriptyline	20 mg.p.o.	1.833**±0.4014
IV	*S. anacardium*	100 mg p.o.	11.167**±0.4014
V	*S. anacardium*	200 mg p.o.	7.833**±0.4014
VI	DKT-SA	40 mg p.o	4.167**±0.4014
	F One-way ANOVA d_f		139.9435

n=6 in each group. Data is expressed as mean ± SEM. Statistical analysis by one-way ANOVA followed by Dunnett's't' test. Significance at P<0.05*, P <0.01**, and ns-not significant *vs.* control group.

TABLE 8: EFFECT OF *S. ANACARDIUM* ON SODIUM NITRITE INTOXICATION MODEL IN MICE

Group no.	Treatment	Dose (Per kg)	Time of Cessation of Respiration in Minutes (Mean ± Sem)
I	Normal control	10 ml p.o.	-
II	Sodium nitrite alone	250 mg i.p.	13.66±0.35
III	Piracetam	200 mg p.o.	32.5±0.50**
IV	*S. anacardium*	100 mg p.o.	21.25±0.22**
V	*S. anacardium*	200mg p.o.	23.76±0.14**
VI	DKT-SA	40 mg p.o.	27.91±0.20**
	F One-way ANOVA D_f		54.91228

n=6 in each group. Data are expressed as mean ±SEM. Statistical analysis by one-way ANOVA followed by Dunnett's't' test. Significance at P<0.05*, P <0.01**, and ns-not significant *vs*. control group.

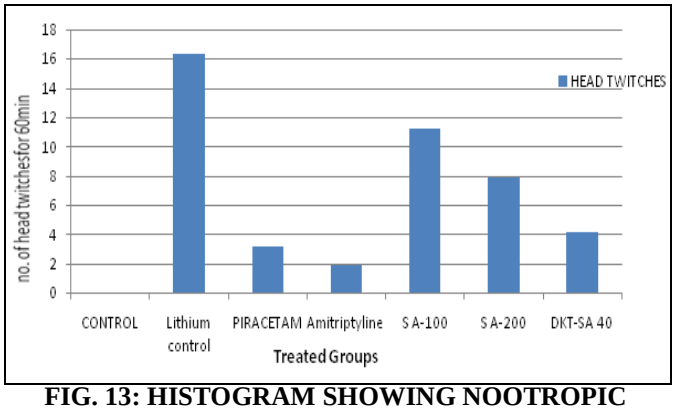

FIG. 13: HISTOGRAM SHOWING NOOTROPIC EFFECT OF *S. ANACARDIUM* ON LITHIUM-INDUCED HEAD TWITCHES IN RATS

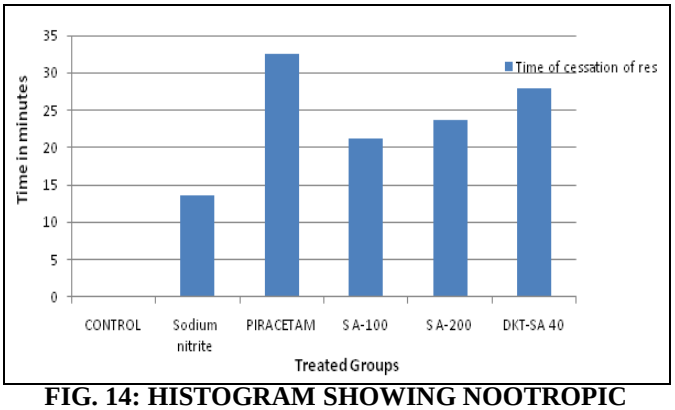

FIG. 14: HISTOGRAM SHOWING NOOTROPIC EFFECT OF S. ANACARDIUM ON SODIUM NITRITE TOXICITIES MODEL IN MICE

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